plete editing process *in vitro*. Encouraging preliminary evidence is now being observed in a number of laboratories.

One outstanding matter likely to be resolved is how the gRNAs guide the editing. Do they precisely dictate each editing modification or do they selectively preserve sites that become correctly edited in a less rigidly directed[6] cleavage/joining system? An understanding of the basis of the developmental regulation of editing should also emerge. And this knowledge may well provide insight into the intriguing evolutionary issues implicit in RNA editing. We can be optimistic that a popular topic for journal clubs a year hence will be the great progress in understanding the mechanism of trypanosome RNA editing that derives from these *in vitro* systems. □

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CLIMATE

Deep ocean circulation puzzle

Rainer Zahn

NOTIONS of the influence deep ocean circulation can have on the climate will have to be revised in the light of papers on pages 757 and 783 of this issue. Lehman and Keigwin[1] and Veum *et al.*[2] have examined tracers of ocean circulation in the northern corner of the North Atlantic and find that changes there 10,000 years ago, when the Earth was emerging from the last Ice Age, were not responsible for sudden, temporary regressions to glacial climes, as has been suggested.

If extremes of behaviour in a system are a good indicator of its underlying processes, then the Younger Dryas cold episode, a brief glacial snap 10,000 years ago during the global warming that brought our planet out of the last Ice Age, is an outstanding clue to the climate's inner workings and an outstanding example of the internal discontinuities it is susceptible to. Although external forcing such as solar heating increased gradually towards warmer conditions, the associated climatic transition was far from running smoothly. Several climatic anomalies are documented for this transition, the most severe being the Younger Dryas (named after *Dryas octopetala*, a flower typical of polar climates). Impressed by its apparent abruptness and severity, oceanographers and climatologists sense that this sharp climatic anomaly, which lasted only a few centuries, may reveal much about the operation of ocean–climate processes. The emergence of high-resolution accelerator techniques for dating sediments and microfossils in the mid-1980s provided an essential pre-requisite for studying such abrupt climate change and triggered a bloom of research on the Younger Dryas (see the accompanying chronology).

At the heart of the problem lies the way the North Atlantic Ocean circulated during various phases of the last glacial–interglacial transition. In the modern ocean, flow of warm saline surface waters from the tropical and subtropical Atlantic to the high-latitude North Atlantic, accompanied by evaporation (and so cooling and increased salinity), is apparently required to trigger sinking of dense polar surface waters and formation of North Atlantic deep water. Advection of surface waters from the south, subsequent sinking and horizontal escape at depth may be viewed as a self-sustaining circulation loop which is part of the larger-scale water mass exchange between the North Atlantic and the rest of the world's oceans. The driving force which keeps this so-called "conveyor belt circulation"[3] in motion is the flux of density due to the transport of salt through the North Atlantic[4,5]. Modulations of the conveyor belt due to varying inputs of meltwater from disintegrating ice sheets have been called upon to explain the Younger Dryas climatic deterioration during the global warming of the last deglaciation[3]. The injection of meltwaters would overwhelm freshwater loss from surface waters by evaporation and lower the salinity of North Atlantic surface waters to an extent that the density contrast between surface waters and underlying deep waters becomes too large to be compensated by winter-time cooling at the surface. Water convection would cease and the conveyor belt would become drowned out of existence. Because warm saline tropical waters would stop flowing into the subarctic North Atlantic, climate in the region would deteriorate to almost fully glacial conditions.

Meltwater discharge into the North Atlantic did not continue evenly over the last glacial–interglacial transition (between 14,000 and 8,000 years ago). There were two meltwater pulses, separated by about 2,500 years, from distinct episodes of disintegration of the North American Laurentide Ice Sheet[6]. The Younger Dryas cold episode started just after the first meltwater pulse and ended shortly before the second one: instead of happening alongside elevated meltwater input, the Younger Dryas is centred right in the low between the two pulses, when melting came close to a halt.

This is exactly what Lehman and Keigwin[1] observe by looking at microfaunal and stable-isotope distribution patterns along a highest-quality sediment core with extraordinarily high sedimentation rates. Their data imply that times of minimum meltwater supply correlate with periods of cooling. This does not sound so alarming, as cooling is expected to halt melting. But the point is that, according to the conveyor-belt hypothesis, the halt in meltwater flow should result in warming, by starting off salt buildup and sinking of surface waters with the subsequent inflow of warm surface waters from the south.

This theory had already been challenged by two palaeoceanographers, Jansen and Veum[7] from Bergen, who used microfossil carbon isotope data (a reliable tool for reconstructing deep water circulation) to suggest that deep convection continued in the North Atlantic even during the Younger Dryas cold period. Apparently, this convection failed to draw warm waters from the south into the polar North Atlantic. Now Veum *et al.*[2] use another record from a coring site further north to show that ventilation of the deeper water column in the Norwegian–Greenland Sea was probably as vigorous during the Younger Dryas as it is today. Their first carbon isotope record looked somewhat spurious, but with the new data one has to take this conflicting evidence seriously.

It is unlikely that Lehman and Keigwin are off the track because, first, the very high sedimentation rates of 5 metres per 1,000 years at their core site (compared with 2–5 centimetres per 1,000 years at open-ocean core sites) rule out the possibility of significant

1. Lehman, S. J. & Keigwin, L. D. *Nature* **356**, 757–762 (1992).
2. Veum, T., Jansen, E., Arnold, M., Beyer, I. & Duplessy, J. C. *Nature* **356**, 783–785 (1992).
3. Broecker, W. S. *et al. Paleoceanography* **5**, 1–19 (1988).
4. Broecker, W. S. *et al. Palaeoceanography* **5**, 469–477 (1990).
5. Birchfield, G. E. & Broecker, W. S. *Paleoceanography* **5**, 835–843 (1990).
6. Fairbanks, R. G. *Nature* **342**, 637–642 (1989).
7. Jansen, E. & Veum, T. *Nature* **343**, 612–616 (1990).
8. Dansgaard, W. *et al. Nature* **339**, 532–534 (1989).
9. Martinson, D. G. *et al. J. phys. Oceanogr.* **11**, 466–488 (1981).
10. Boyle, E. A. & Keigwin, L. D. *Nature* **330**, 35–40 (1987).
11. Charles, C. D. & Fairbanks, R. G. *Nature* **355**, 416–419 (1992).
12. Labeyrie, L. D. *et al. Quat. Sci. Rev.* (in the press).
13. Sarnthein, M. & Tiedemann, R. *Paleoceanography* **5**, 1041–1055 (1990).
14. Schlosser, P. *et al. Science* **251**, 1054–1056 (1991).
15. Emiliani, C. *et al. Earth planet. Sci. Lett.* **41**, 159–162 (1978).
16. Ruddiman, W. F. & McIntyre, A. *Palaeogeogr. Palaeoclimatol. Palaeocol.* **35**, 145–214 (1981).
17. Kallel, N. *et al. Oceanol. Acta* **11**, 369–375 (1988).
18. Bard, E. *et al. Quat. Res.* **31**, 381–391 (1989).
19. Shackleton, N. J. *Nature* **342**, 616–617 (1989).
20. Engstrom, D. R. *et al. Science* **250**, 1383–1385 (1990).
21. Kudrass, H. R. *et al. Nature* **349**, 406–409 (1991).
22. Keigwin, L. D. *et al. J. geophys. Res.* **96**, 16,811–16,826 (1991).

stratigraphical distortions; and, second, their records are well-dated and are correlated directly with similar climatic evidence drawn from the Greenland Dye-3 ice core. The dramatic short-term climatic oscillations documented in the ice core[8] affected the regional climates all the way over to Northwest Europe.

The combined deep-ocean oxygen and carbon isotope data shown by Veum *et al.* imply that large parts of today's subpolar North Atlantic froze over during the Younger Dryas. The forming sea ice rejects salt, so increasing surface-water salinity, which apparently resulted in a density flux large enough to ventilate the deeper water column at least as effectively as today. Clearly, this evidence must be confirmed. If the data can be reproduced at other coring locations and still show that open-ocean convection occurred even during the coldest periods of the Younger Dryas — when the conveyor belt was supposedly switched off — climate modellers will have to deal not only with the ons and offs of the conveyor but possibly also with switches between cold and warm conveyors. The correlation of core data from the Norwegian–Greenland Sea with those from the shallow North Atlantic seems to imply that during the Younger Dryas the cold conveyor belt operated at shallower depth than today's warm belt. The driving force behind the cold belt would be a gradual buildup of salinity during sea-surface freezing, which would resemble the mechanism which starts off deep convection in today's Southern Ocean[9]. This factor is not accounted for by the concept of salt transport through heat and vapour flux[4,5] and, frankly, it sounds rather far-fetched. Yet the data exist and must be confronted.

An obvious shortcoming of the conveyor-belt/salt-flux hypothesis is that it deals with mean-ocean conditions and North-Atlantic mean flow rates. Thermohaline circulation is driven by regional and seasonal anomalies in the ocean's temperature–salinity field. The main sites of convection which feed today's conveyor belt are located in very restricted areas in the Norwegian–Greenland Seas and the Labrador Sea. In these areas convection occurs mainly during winter time. One may argue that this dependency on sinking of water masses in restricted provinces would make the conveyor belt even more vulnerable to large-scale meltwater input. Still, it seems that even during times of highest meltwater input immediately before and after the Younger Dryas, the deep North Atlantic was better ventilated than during the Younger Dryas[10], which may have been meltwater-free[6].

It seems critical to finding a solution for this circulation puzzle to determine

Chronology of Younger Dryas research

LATE 1970s TO EARLY '80s Dominance of polar foraminiferal populations implies nearly full-glacial conditions during the Younger Dryas which may be caused by rapid meltwater injection during the initial disintegration of continental ice sheets[15,16].

1987

NOVEMBER Geochemical evidence arises for extremely low ventilation of the deep North Atlantic during the Younger Dryas, implying a shut-down of water-mass sinking in the North Atlantic and a halt of the conveyor belt[10].

1988

FEBRUARY Meltwater signals in sediment cores from the Gulf of Mexico and the subarctic North Atlantic imply a diversion of meltwater flow from the Gulf to the North Atlantic before and during the Younger Dryas. Poleward flow of warm waters in the conveyor belt was cut off causing the Younger Dryas climatic collapse around the North Atlantic[3].

OCTOBER Stable isotope and planktonic faunal records from a Northwest Pacific sediment core show a cooling event synchronous with the Younger Dryas. The data suggest that the Younger Dryas was not restricted to the North Atlantic and that the cooling took in the high-latitude North Pacific[17].

1989

MAY A drop in North Atlantic surface water temperature by almost 10 °C during the Younger Dryas is indicated by changes in the planktonic community structure[18] and seems to be consistent with a conveyor-belt switch-off mode.

JUNE Geochemical tracers and airborne dust embedded in Greenland ice layers show the North Atlantic climate shifted 'back to normal' in less than 20 years at the end of the Younger Dryas[8].

DECEMBER Growth rate curves of reef corals off Barbados point to strongly reduced meltwater inputs to the North Atlantic during the Younger Dryas. The hypothesis that increased meltwater discharge into the North Atlantic is the cause of the Younger Dryas comes under fire[6,19].

1990

FEBRUARY Benthic and planktonic isotope data from a northeast Atlantic sediment core imply increased deep water formation and ventilation of the deeper water column during the Younger Dryas, further undermining the meltwater hypothesis[7].

AUGUST In a revision of the meltwater hypothesis, a salt oscillator is designed which turns the conveyor belt on and off. The strength of the conveyor belt no longer depends on the rate of deglacial meltwater input, as the primary force is now heat flux and vapour transport[4].

DECEMBER Numerical modelling of the salt oscillator suggests that North Atlantic surface salinity may fluctuate at periods of a few thousand years. The model does not test the sensitivity of salt oscillations to regionally variable meltwater inputs[5].

Long time series of benthic isotope records show Younger-Dryas type climatic reversals during six deglacial transitions of the past 700,000 years. Each was supposedly accompanied by a temporary shut-down of deep-water production in the North Atlantic pointing to a switch-off of the conveyor belt[13].

Pollen records from southeastern Alaska document a cooling event which may have been coeval with the Younger Dryas; the Younger Dryas was a possibly hemisphere-wide event[20].

1991

JANUARY Deglacial climate breakdowns are observed in isotope records from two Sulu Sea sediment cores and are used to infer that the Younger Dryas was a global event caused by lowered atmospheric CO_2 concentrations[21].

SEPTEMBER High-resolution palaeochemical records from the North Atlantic reveal periodic decreases in deep-water production during deglaciation at roughly the same periods as predicted from the salt-oscillation model. Decreased ventilation of the deeper water column during the Younger Dryas suggests the conveyor belt was switched off as North Atlantic surface salinities decreased, owing to meltwater input or cooling[22].

1992

JANUARY Comparison of geochemical records obtained from North Atlantic and Southern Ocean sediment cores implies a significant influx of North Atlantic water masses to the Southern Ocean even during the Younger Dryas[11] — the conveyor belt remained switched on.

APRIL High-resolution geochemical and plankton data imply a rapid shut-down of circulation during the Younger Dryas in the North Atlantic[1], but benthic isotope data from the same region suggest that deep ventilation continued and was probably as vigorous as today[2].

whether thermohaline circulation truly behaves like a conveyor belt that shuts on and off, or whether the sites of convection shift between different locations as the salt oscillator pushes the subpolar North Atlantic from one mode to another. Perhaps the conveyor was never really switched off but operated at shallower depth. That way the deep Atlantic would not see the lower limb of the belt, but the North Atlantic would still be flushed with young waters. Then water from the North Atlantic could have reached the Southern Ocean even during the Younger Dryas, as indicated by the coherent development of geochemical proxies along sediment cores from both ocean basins[11]. With more high-quality data from throughout the subpolar North Atlantic the evolution of regional anomalies and their thermohaline momentum should become apparent[12]. Special emphasis should be put on the other glacial–interglacial transitions of the past 700,000 years, which had their own Younger-Dryas type breakdowns[13].

In view of impending global warming, progress in understanding this type of climate collapse is needed urgently. As recent work has shown[1,8], once the trigger has been pulled, North Atlantic climates can change dramatically within less than 50 years. And it seems[14] that since the early 1980s a slow-down of deep convection in the Greenland Sea has already been under way. □

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T-CELL RECEPTORS

At grips with interactions

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DURING the 1980s the riddle of the T-cell antigen receptor (TCR) was solved, revealing a two-chain structure like an antibody Fab fragment with a binding surface likely to be constructed from hypervariable loops of the TCR Vα and Vβ domains. This surface is proposed to interface with the top of the MHC molecule including foreign peptide bound in a groove formed by two α helices. The TCR, however, remained a receptor whose binding was inferred but not quantified.

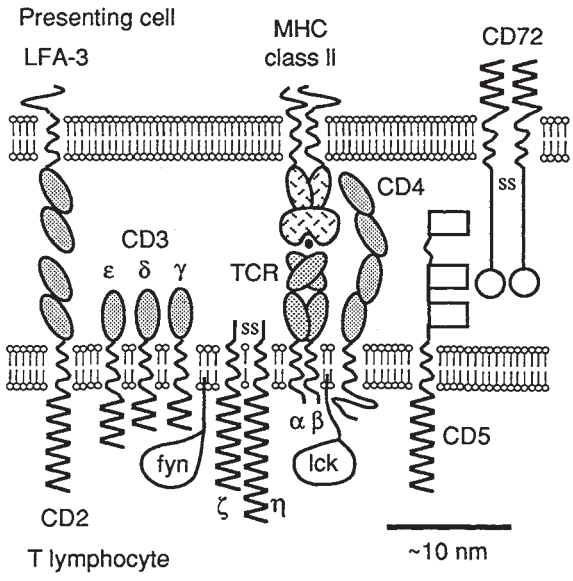
This deficiency has now been rectified in two studies, one published in *Science*[1], the other reported on page 793 of this issue[2], where the binding affinity of TCRs has been measured. Matsui *et al.*[1] measured TCR binding affinity by determining the amount of soluble MHC class II antigen loaded with a relevant peptide (henceforth called 'MHCpep') that was needed to block binding of an anti-TCR Fab of known affinity to cell-borne TCR. From this data K_{equil} for the TCR was calculated to be about 2×10^4 M^{-1}. Weber *et al.*[2] blocked T-cell responses with soluble forms of TCR and calculated a value of about 10^5 M^{-1}. Thus the independent studies are in quite good agreement, with both giving a low affinity of the order of the lowest known antibody reactions for binding. High affinities for antibody binding are due to somatic mutations as an immune response matures, and as the TCR does not undergo somatic mutation it seems that the current values should be taken as typical for TCR reactions.

Two other numbers are relevant in thinking about T-cell reactions. One is the likely time for 50% dissociation of monovalent TCR:MHCpep reactions (the $t_{1/2}$ value). By comparison with a typical antibody this is calculated to be 0.3 seconds (the OX7 Anti-Thy-1 Fab has a K_{equil} of 3×10^9 M^{-1} and $t_{1/2}$ of 8,400 seconds; the TCR $t_{1/2}$ value is calculated from an affinity of 10^5 M^{-1} assuming an on-rate similar to OX7 Fab). The other relevant number is the number of MHCpep complexes that are needed to trigger a cell, which has been measured in the range of 50–300 molecules per cell[3,4].

What constraints do these numbers place on how the TCR may function? First, the binding energy between TCR and MHCpep must be a trivial factor in adhesion reactions between T cells and presenting cells. For example, a TCR contribution would surely be swamped by that of CD2:LFA3 binding alone, because there are about 5×10^4 molecules of CD2 per resting T cell and the K_{equil} for the CD2:LFA3 interaction has been measured at 2.5×10^6 M^{-1} (ref. 5). In fact, if the situation *in vivo* is considered, the concept of a T cell in one corner of a dish needing to find a presenting cell at another becomes nonsensical. *In vivo* a T lymphocyte in the blood leaves the bloodstream by interaction with the vascular endothelium and from then on will travel through a lymph node in a manner in which contact with other cells is always maintained. So the concept of bringing cells together changes to one of triggering and guiding the movement of the T cell through the node.

Possibly, the molecules we refer to as adhesion molecules are the ones that determine the preferences of cell interactions and the pathways of movement. The T cell may move over cells that present no relevant antigen so that the recirculatory pathway is completed uneventfully. But if relevant MHCpep is presented, the TCRs bind and trigger the cell. Thus one can think of a cell moving along and receiving signals from its TCRs as it goes. If the TCRs achieve a sufficient firing rate, gross changes in the cell occur. Adhesion reactions are known to be strengthened after T-cell activation[6], and one can imagine cell movement ceasing and the activated T cell engaging in further interactions with the presenting cell from which the triggering signals were received. The TCR can be expected to play a crucial role in all of this, not by virtue of the contribution that its binding energy makes to cell–cell adhesion but because it triggers the cell in a way that leads to qualitative changes in its state.

The quantitative parameters of the TCR reactions are also relevant to concepts of triggering by way of the TCR. It is generally thought that TCRs must be crosslinked to activate a T cell, yet how is this to occur through the TCR:MHCpep interaction? It seems most improbable that adjacent MHC molecules will display the same peptides, and to give a crosslinking signal two MHC molecules displaying the same peptide would have to be tethered together. With $t_{1/2}$ values of the order of seconds for the TCR reactions, and very small numbers of molecules involved, is



A T cell interacting with a presenting cell, showing molecules that are likely to exist in a T-cell activation complex for a T lymphocyte restricted by MHC class II antigen[7].